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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,913	10/23/2006	Hyae Gyeong Cheon	DE1700PCT	6550

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EXAMINER	
BAEK, BONG-SOOK	
ART UNIT	PAPER NUMBER
4161	
MAIL DATE	DELIVERY MODE
07/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,913	CHEON ET AL.	
	Examiner	Art Unit	
	BONG-SOOK BAEK	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *5-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/18/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of claim

Claims 1-9 are currently pending.

Election/Restrictions

Applicants' election of group I drawn to a compound of a indene derivative defined by formula (I) and election of the following species: 1-hydroxy-6-(2-morpholine-4-ylethoxy)-1, 3-diphenyl-1H-indene -2-carboxylic acid ethyl ester, in the reply filed on 6/5/2008 are acknowledged.

The above election was made without traverse. Claim 5-7 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group. The elected species is free of prior art, thus examination is further extended the next species. Claims 1-4 and 8-9 are under examination in the instant office action.

Priority

The instant application is a 371 of PCT/KR05/01051 filed on 4/12/2005 and acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). A certified copy of foreign application filed on 4/13/2004 has been submitted on 10/13/2006.

The earliest effective U.S. filing date of the instant invention has been determined to be 4/12/2005.

Information Disclosure Statement

A signed and initialed copy of the IDS filed on 4/18/2008 is enclosed in this action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 8-9 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a few compounds of formula (I), does not reasonably provide enablement for plethora of possibilities encompassed by the formula (I). With respect to the making aspect of enablement requirement, the specification is enabling for making compounds recited in claim 4. It is not seen where in the specification enablement is for compounds other than the preferred compounds recited in claim 4. With regards to use aspect of the specification, the disclosure is limited to the results of receptor binding activity of limited number of compounds for only peroxisome proliferator-activated receptor-γ (PPAR-γ) and a biological activity for only elected species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the relevant factual considerations.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). While all the above factors were considered, some of the specific considerations are described below:

The breadth of the claims: The claim is drawn to compounds defined by formula (I), which are allegedly useful in the treatment of a variety of disorders. The formula (I) is drawn to constituents layered on top of constituents that vary independently and lead to compounds of a wide variety of structures. These compounds encompass molecules that widely vary in the physical and chemical properties such as size, molecular weight, acidity and passivity, properties that are known in the art to greatly influence pharmacokinetic and pharmacodynamic parameters, not to mention the ability to productively bind to claimed biological target molecules. The number of theoretically conceivable compounds for the formula is in billions rendering the scope of the claims large.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for viability.

The amount of direction or guidance present: The guidance and direction provided in the application for making the claimed compounds is limited. The direction is limited to preferable embodiments. That is, the applicant, at the time of the instant application, was in possession of those preferable embodiments. Thus, one skilled in the art attempting to make all the compounds of the present inventions would face with undue research burden.

The state and the predictability of the art: The pharmaceutical art is unpredictable and target compounds need to be individually assessed for viability. The instant invention is directed

to compounds which allegedly have modulating peroxisome proliferator-activated receptor (PPARs) and can be used for the treatment of various disorders such as diabetes, obesity, atherosclerosis, hyperlipidemia, hypertension, osteoporosis, liver cirrhosis, asthma, and cancer. PPARs are a group of nuclear receptor proteins that function as transcription factors regulating the expression of genes and play essential roles in the regulation of cellular differentiation, development, and metabolism (carbohydrate, lipid, and protein) of higher organisms. There are three types of PPARs, alpha, gamma, and delta, which are expressed in different levels in different tissues and have different physiological effects (Berger *et al.*, Annu Rev Med, vol. 53, p409-435, 2002). Therefore, based on which subtype of PPARs is modulated by the claimed compounds, different outcome would be resulted in. Eextremely broad generalizations as found in the instant claims are in contradiction with the basis of quantitative structure-activity-relationship (QSAR). In addition, in spite of the narrow structural characteristics (see above) of the disclosed compounds, the biological activity seems to vary widely. Thus it is unpredictable what specific embodiment of the billion possibilities of the instant claims would have the desired biological properties.

The quantity of experimentation needed: Based on: a) claims to widely varying structures encompassed by the formula (I), b) lack of disclosure with respect to structural requirement for compounds to modulate PPARs (i.e. pharmacophore), and c) applicant's characterization of what is considered 'biologically active', one of ordinary skill in the art would be presented with an unpredictable amount of research effort to identify a compound out of the plethora of possibilities encompassed by the formula I that would have useful biological properties.

Genentech Inc. v. Novo Nordisk A/S (CA FC)42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

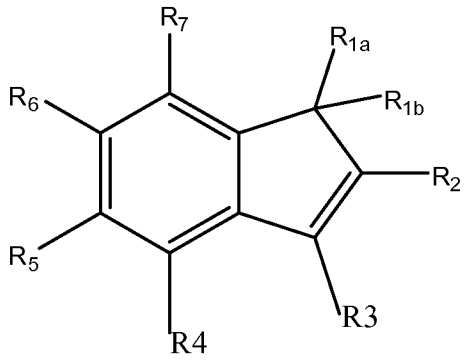
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

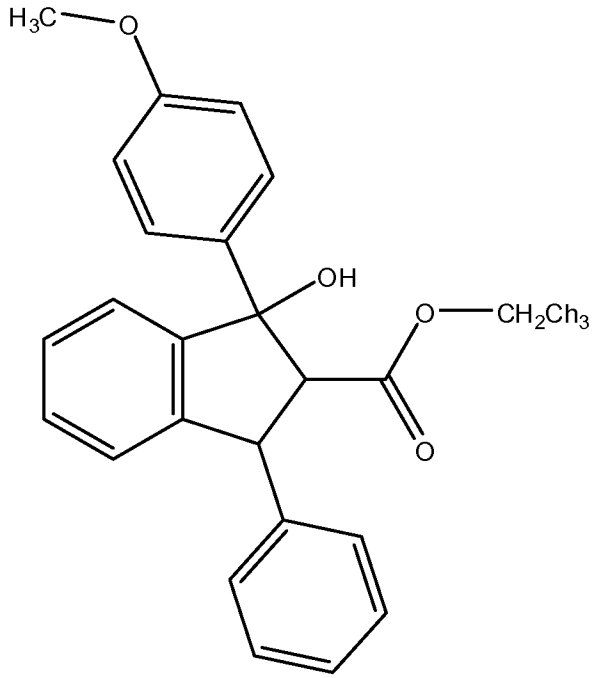
Claims 1-2 and 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9308799 (Pub. Date: 5/13/1993). WO 9308799 is supplied by applicant on IDS filed on 4/18/2008.

The instant invention is drawn to an indene derivative represented by the following formula (I) and a pharmaceutical composition comprising an indene derivative represented by formula together with a pharmaceutically acceptable carrier.



Formula (I)

WO 9308799 discloses indene derivatives with the same core structure as recited in the instant invention encompassing the species claimed in the instant invention (claim 1). In particular, the following compound, which is a species of the instant invention, is disclosed in WO 9308799 (p20, lines 14-15)



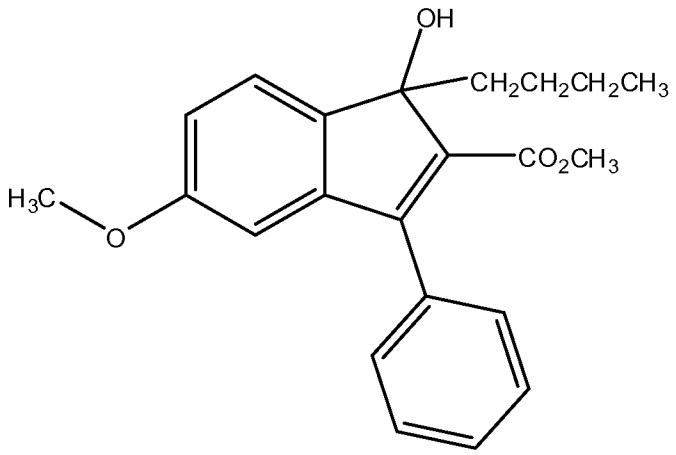
1-hydroxy-1-(4-methoxyphenyl)-3-phenyl-1H-Indane-2-carboxylic acid ethyl ester

The reference also teaches a pharmaceutical composition of an indene derivative (p15, lines 20-36). In addition, since the instant claims 8-9 are directed to a composition, an intended use, which is for modulating the activities of paroxysm proliferators activated receptors and for the treatment and prevention of diabetes (elected species), does not have a patentable weight. In accordance with the patent statutes, an article or composition of matter, in order to patentable, must not only be useful and involve invention, but must also be new. If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or

composition, regardless of the use for which it is intended. The difficulty is not that there can never be invention in discovering a new process involving the use of an old article, but that the statutes make no provision for patenting of an article or composition which is not, in and of itself, new. As such, the instant claims are anticipated by WO 9308799.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Rayabarapu *et al.* (J. Org. Chem., vol. 68, p6726-6731, 2003).

Rayabarapu *et al.* teach the following indenol derivatives encompassing generically claimed compounds of the instant invention (p6727, table 2, entry 16).



1-hydroxy-6-methoxy-1-n-butyl-3-phenyl-1H-Indane-2-carboxylic acid methyl ester

As such, the instant claims are anticipated by Rayabarapu *et al.*

Claim Rejections - 35 USC § 103

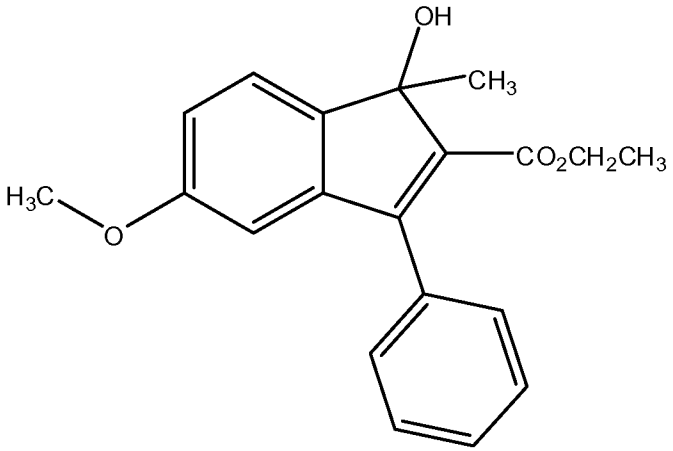
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

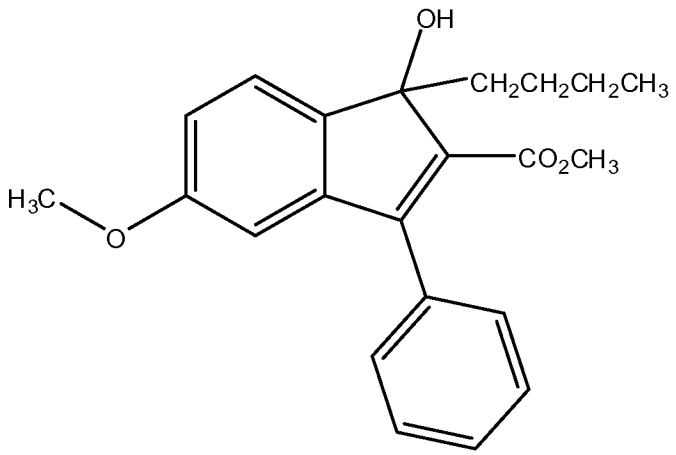
Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rayabarapu *et al.*

The following compound is recited in the instant claim 4.



1-hydroxy-6-methoxy-1-methyl-3-phenyl-1H-Indane-2-carboxylic acid ethyl ester

Rayabarapu *et al.* teach the following indenol derivatives encompassing generically claimed compounds of the instant invention (p6727, table 2, entry 16) as stated above.



1-hydroxy-6-methoxy-1-n-butyl-3-phenyl-1H-Indane-2-carboxylic acid methyl ester

The difference between the instant compound and that of the prior art is that the instant compound has methyl group instead of butyl in the position 1 and is ethyl ester rather than methyl ester.

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to substitute n-butyl with methyl and to make methyl ester instead of ethyl ester since it is common to substitute one C_{1-5} alkyl group with another C_{1-5} alkyl group in the field of organic chemistry. One skilled in the art at the time the invention was made would be obvious to be motivated to make analogs of Rayabarapu *et al.* to arrive at other biologically active indenol compounds with reasonable expectation of success since Rayabarapu *et al.* teach indenol moiety is an important and central structural unit present in various biologically active compounds (p6726, left column 1st paragraph).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached 8:00-5:00 Monday-Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BONG-SOOK BAEK
Examiner, Art Unit 4161

Bbs

/Patrick J. Nolan/

Supervisory Patent Examiner, Art Unit 4161